DETAILED ACTION

1. Currently, claims 1-11,16-18,21-25,27-31,55-57,61-63 and 66-71 are pending in the instant application. Claim 12-15, 19-20, 26, 32-54, 58-60 and 64-65 have been canceled. This action is written in response to applicant's correspondence submitted 4/1/2011. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is Final.**

Maintained Rejection

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-11, 16-18, 21-25, 27-31, 55-57, 61-63, 66-71 rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (PCT WO95/02049) in view of Nieuwkerk et al. (US Patent 5438128). This rejection is reiterated from the previous office action and is reiterated below.

Jones (WO95/02049) teaches a method of purifying DNA (biological macromolecule) from *E. coli* bacterial culture (biological sample) by passing the cells through a 1 μm filter followed by a 20μm filter (page 22, 1st full paragraph). Jones et al. teaches that the method can be used for genomic DNA (see page 4, 1st paragraph).

With regard to claim 2, Jones teaches the method of purifying nucleic acid from cells that comprises lysing a cell suspension to form a cell lysate containing nucleic acid and applying the cell lysate to a filter to remove unwanted cells and cell debris (page 2, 4th full paragraph).

With regard to claims 3-5, Jones teaches that any cell producing a target compound may be used in their invention. Jones defines a "cell" to encompass bacterial cells, cells from higher organisms for example blood cells, phage particles, and other cell types or organelles which contain the target compound and may require some form of lysis step to release it (page 3, 4th full paragraph). The cells are lysed prior to applying to the first filter (page 2, 4th full paragraph).

With regard to claims 6-11, Jones teaches that the target compound to be separated may comprise nucleic acid (instant claim 6), protein, or other desired compounds, in particular purifying recombinant proteins and antibodies (instant claim 7)(page 2, 2nd and 3rd paragraph). Jones further teaches that RNA or DNA may be purified using this invention (page 5, 2nd paragraph) (instant claim 8-11).

With regard to claims 16-18, Jones teaches the use of two filter layers to purify DNA from bacterial cells, with the first filter having 1μm pore size and the second filter having 20 μm pore size (instant claims 16-18) (page 22, 1st full paragraph).

With regard to claims 21-25, 27, 67-70, Jones teaches the use of a first filter that retains unwanted cells and cell debris (instant claim 21), that is made of any material that can tolerate the reagents such as cellulose acetate (acetylated cellulose) (instant claim 24 and 25) and is no greater than 50 μm in pore size and no smaller than .2 μm (instant claim 22-23) (page 6, 1st full paragraph). Jones teaches that for a nucleic acid, the filter is typically glass or resin based and can bind the nucleic acid such as borosilicate glass (see page 6, 2nd paragraph) (claim 24). Jones teaches that the first filter is no greater than 50 μm in pore size and no smaller than .2 μm (see page 6, 1st paragraph) and the second filter is a 20 μm pore size (see page 22, 1st full paragraph) (instant claim 27).

With regard to claim 28 and 29, Jones teaches the method of a membrane filter that is placed inside the column (tube) (instant claim 29) and has a cylindrical shape (instant claim 28) (page 11, last paragraph, figure 1 and figure 2).

With regard to claims 30-31, Jones teaches the method of lysing a cell suspension to form a cell lysate, applying the cell lysate to a filter to remove unwanted cells and cell debris, contacting the filtered lysate with a solid phase matrix, separating the resultant filtered lysate from the matrix, and eluting the nucleic acid from the matrix (page 2, 4th full paragraph). Jones teaches the method of purifying plasmid DNA by using a filtration method of increasing pore

sizes of two filters using a 1 μm filter followed by a 20 μm filter and promoting the flow of lysate through the filters by positive pressure (page 22, 1st full paragraph).

With regard to claim 55-57 and 61-63, Jones teaches the method of lysing a cell suspension from *E. coli* (natural source) to form a cell lysate, applying the cell lysate to a filter to remove unwanted cells and cell debris, followed by contacting the filtered lysate with a solid phase matrix, separating the resultant filtered lysate from the matrix, and eluting the nucleic acid from the matrix (page 2, 4th full paragraph). Jones teaches the method of purifying plasmid DNA (instant claim 57) by the method of increasing the pore sizes of the filters (instant claim 55), by using a 1 μm cellulose acetate filter followed by a 20 μm PTFE filter (instant claim 61-62) and promoting the flow of lysate through the filters by positive pressure (instant claim 56) (page 22, 1st full paragraph and Table 1, page 21). Jones teaches that for a nucleic acid, the filter is typically glass or resin based and can bind the nucleic acid such as borosilicate glass (see page 6, 2nd paragraph) (claim 63).

With regard to claim 66, Jones et al. teaches two filters that have the inherently property of shearing genomic DNA, as evidenced by applicant's own specification (see page 13, last paragraph to page 14, 1st line).

Jones does not teach that the first and second filter layer is within the same hollow body or comprises a multilayer filter bed.

However, Nieuwkerk et al. teaches a method for convenient and rapid isolation of nucleic acids (see column 2 lines 64-68) which comprises membranes stacked one on top of the other to form a column having a short bed depth (see column 5 lines 52-56) (multilayer filter bed).

Nieuwkirk et al. teaches a device for the isolation of nucleic acids that comprises stacked membranes that have a pore size of .1 to 12 microns and teaches that the preferred number of stacked membranes (first and second filter directly contacting) is from one to 20 (see column 2, lines 28-40). Niewkirk teaches that the stacked membranes provide a short bed length to allow the column to be used with low pressure systems, including a simple vacuum manifold and hand held syringe, as well as the short bed reduces the quantity of eluant required (see column 5 lines 60-65). Further Nieuwkirk teaches the device allows for a small easy to use disposable device (see column 5 lines 40-50). Nieuwkirk et al. teaches plasmid purification by contacting the filter with cell lysate (see example 1, column 8 lines 28-67) (claim 70).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of isolating nucleic acids from cell lysate by using the filter apparatus as taught by Jones et al. to include multiple layer filter bed of filters housed within the same column, as taught by Nieuwkirk, to improve the method by Jones et al. to allow for a simpler, easier to use and disposable column. The ordinary artisan would have been motivated to improve the method of isolating nucleic acid from cellular lysate with the filter taught by Jones to include the filters housed in one column to thereby produce a multilayer filter bed as taught by Nieuwkirk because Nieuwkirk teaches that stacked membranes in a column allows for reduced quantity of eluant and use with low pressure systems, as well as provides a small, easy to use disposable device. The ordinary artisan would have had a reasonable expectation of success that the method of nucleic acids from cellular lysate of Jones modified to house the filters in one unit to produce a multilayer filter bed in the same hollow

body, as taught by Nieuwkirk because Nieuwkirk et al. teach that multilayer filters can be used to isolated nucleic acid from cellular debris (see example 1).

Response to Arguments

5. The response traverses the rejection on page 8 of the remarks mailed 4/1/2011. The response asserts the claims have been amended to recite that second filter layer allows said biological macromolecules to pass. The response asserts that Jones passes the target molecule through the first filter but not through the second filter but rather binds the target molecules to the second matrix instead of passing it through and Jones necessarily includes an elution step. The response asserts that the claimed method are performed without an elution step. This response has been thoroughly reviewed but not found persuasive. Initially it is noted that the claims do not exclude the target nucleic acid from binding to any filter, for example the claims do not exclude the target nucleic acid from binding to the second filter, as taught by Jones. The amendment to the claims recite that the second filter layer allows said biological macromolecules to pass thus the biological macromolecules may pass during an elution step and therefore the claims do not exclude an elution step. The claims do not require that the nucleic acid is purified without an elution step, the claims merely require that the first filter layer retains cellular debris, second filter layer allows said biological macromolecules to pass and biological macromolecules are isolated and thus the macromolecules are allowed to pass through the second filter layer, which could occur via elution, which is taught by Jones . With regard to applicants response that Niewkerk does not remedy the defiency of Jones, it is noted that Niewkerk was not cited to teach the specific types of filters or membranes but was cited to teach placing multiple filters and membranes in one column to render obvious the method of DNA isolation using the filter

apparatus of Jones et al. with the filter apparatus assembled into a cartridge housing and multilayer filter bed taught by Niewkerk to provide an small easy to use disposable device for DNA isolation.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

6. No claims are allowable.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571)272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Sarae Bausch/
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